

ABSTRACT OF THE INVENTION

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The invention is directed toward a human glycoprotein hormone having at least one, two, three, four, or five basic amino acids in the α -subunit at positions selected from the group consisting of positions 11, 13, 14, 16, 17, and 20. The invention is also directed to a human glycoprotein where at least one of the amino acids at position 58, 63, and 69 of the β -subunit of the human thyroid stimulating hormone are basic amino acids. The invention is further directed to a modified human glycoprotein hormone having increased activity over a wild-type human glycoprotein hormone, where the modified human glycoprotein comprises a basic amino acid substituted at a position corresponding to the same amino acid position in a non-human glycoprotein hormone having an increased activity over the wild-type human glycoprotein hormone. The invention is also directed to a method of constructing superactive nonchimeric analogs of human hormones comprising comparing the amino acid sequence of a more active homolog from another species to the human hormone, and selecting superactive analogs from the substituted human hormones. The invention is also directed to nucleic acids encoding the modified human glycoprotein hormones, vectors containing those nucleic acids, and host cells containing those vectors.